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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,512	12/12/2003	Salman Al-Mahmood	1414-03	6845
35811 7590 01/25/2007 IP GROUP OF DLA PIPER US LLP ONE LIBERTY PLACE 1650 MARKET ST, SUITE 4900 PHILADELPHIA, PA 19103			EXAMINER MCGARRY, SEAN	
			ART UNIT	PAPER NUMBER
			1635	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/25/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.		Applicant(s)	
	10/735,512		AL-MAHMOOD, SALMAN	
	Examiner		Art Unit	
	Sean R. McGarry		1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 7-18 and 21-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 19, 20, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/12/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's election without traverse of Group II, claims 1-6, 19, 20, 26, and 27 in the reply filed on 11/03/06 is acknowledged.

The restriction requirement between the sequences recited in the claims has been withdrawn in part. SEQ ID NOS: 2-23 have all been examined since these sequence all contain significant overlap of sequences. SEQ ID NO: 28 is withdrawn.

Claims 7-18 and 21-25 and SEQ IDNO: 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/03/06.

Information Disclosure Statement

The information disclosure statement filed 12/12/03 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered except

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for the Surmacz et al. reference since the examiner obtained a copy of that reference to apply as prior art.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on 6/14/2001. It is noted, however, that applicant has not filed a certified copy of the French application as required by 35 U.S.C. 119(b).

Claim Objections

Claims 1 and 2 are objected to because of the following informalities: Claim 2 recites non-elected subject a matter [(i) in claim 1 and SEQ ID NO: 28 in claim 2] . Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-6, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 4, 26, and 27 all recite "or derivatives thereof". The recitation of these terms is unclear in two ways. First, it is unclear if the term refers to the "twelve contiguous nucleotides" or to the recited SEQ ID NOS. Second, it is not clear what compounds would be embraced by the term "derivatives". It is not clear to what extent a compound can be "derived" and still be embraced within the instant claims. This is because there is not clear definition of the terms such that the metes and bounds of the claim have been clearly set. If applicant believes that the specification does provide a specific definition, applicant should point to the definition with particularity. Claims 5 and 6 are rejected as far as they depend from claim 4.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Surmacz Clinical Cancer Research Vol. 1.

Surmacz et al disclose an antisense composition that was administered to MCF-7 cells. The antisense composition comprises an antisense oligonucleotide that comprises at least 12 nucleotides that bind to SEQ ID NO: 28 at the nucleotides downstream of the start codon, for example.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Wolf et al [The Journal of Biological Chemistry Vol. 270 (46):27404-27410, 1995].

Wolf et al disclose the human IRS1 cDNA in vectors (see "Material and Methods" section, for example). The vectors disclosed would comprise the SEQ IDS recited in the claims since the vectors are double stranded and the recited SEQ ID NOS are from the human IRS1 sequence.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Surmacz et al, Nolan et al [Int. J. Cancer Vol. 72:828-834, 1997], and Bennett et al [US 5,998,148].

The claimed invention is drawn to a pharmaceutical composition comprising an antisense molecule that inhibits IRS1 expression including and IRS1 of SEQ ID NO: 28 where the antisense is an antisense sequence of a coding region of SEQ ID NO:28 that has at least 12 contiguous nucleotides. The invention also includes where the composition comprises a range of active ingredient capable of specified modes of delivery, and also where the composition comprises a pharmaceutically acceptable carrier.

Surmacz et al disclose an antisense composition that was administered to MCF-7 cells. The antisense composition comprises an antisense oligonucleotide that comprises at least 12 nucleotides that bind to SEQ ID NO: 28 at the nucleotides downstream of the start codon, for example. Surmacz has taught the administration of antisense oligonucleotides at a concentration of 80micrograms/ml and at 120micrograms/ml to inhibit expression of IRS1 in breast cancer cells. Surmacz et al disclose that over expression of IRS1 may play an important role in the loss of hormone dependence of breast cancer cells and contribute to the phenotypic changes associated with malignant progression

Nolan et al disclose the inhibition of IRS1 expression in breast cancer cells via vectors that express anti-irs-1 clones. Nolan et al indicate that IRS1 may regulate the proliferation of tumor cells, see page 828, for example. Nolan et al have shown that

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significant reduction of IRS1 levels in breast cancer cells results in apoptotic cell death (see pages 831-832, for example).

The above references have shown that the art has used antisense compounds in the research of a biochemical pathway involving IRS1 and breast cancer cells. The prior art has shown that inhibition of IRS-1 in breast tumor cells results in apoptotic cell death of the cancer cells. The prior art above does not specifically disclose the use of pharmaceutical carriers.

Bennett et al teaches that at the time of invention the art was replete with pharmaceutically acceptable carriers that could be used in cell culture to enhance antisense uptake and used in *in vivo* applications. Bennett et al have disclosed at column 5 that antisense compounds are commonly used as research reagents to determine the function of genes and to distinguish between functions of various members of a biological pathway. At column 5 it is also disclosed that antisense oligonucleotides have been employed for therapeutic uses. At columns 12-25 a multitude of carriers are disclosed for the artisan to choose from. One in the art would have know at the time of filing, based on the disclosure of Bennett et al that dosages are routinely established for the particular application at hand and also that one would choose an appropriate carrier for the application at hand. One in the art interested in inhibiting IRS-1 in cells in culture or in an animal model of breast cancer would clearly have an arsenal of well know carriers from which to choose.

The combination of references above clearly show the claimed invention. One in the art would clearly have been motivated to use antisense compositions to determine

IRS1 function in at least breast cancer cells in culture and further would be motivated to make such compositions to test in animal models of cancer, for example.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Claims 19 and 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Surmacz et al, Nolan et al [Int. J. Cancer Vol. 72:828-834, 1997], and Bennett et al [US 5,998,148] as applied to claims 1, 3, 5, 6 above, and further in view of Wolf et al.

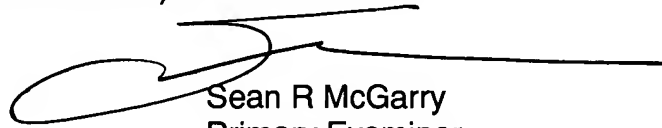
Surmacz et al, Nolan et al [Int. J. Cancer Vol. 72:828-834, 1997], and Bennett et al [US 5,998,148] are relied upon as above and further it is noted that Surmacz et al disclose that the human and mouse sequences of IRS1 are 90% identical and that because of this conserved structure the mouse IRS-1 is fully functional in human breast cancer cells. It is also noted that the vectors used by Nolan et al contained the mouse antisense sequence. Wolf et al disclose that the human sequence was known. It clearly would be obvious to use a human IRS sequence expressed in the antisense orientation to inhibit human IRS-1 expression. It appears that it was a matter of convenience for the artisenns to use a construct already made an avialble for use in human breast cancer cells, but clearly the use oof a human antisense sequence to inhibit a human sequence would be an obvious option. It is noted that the specified sequences of claim 19 would all be comprised in an antisense expressed from a human antisense IRS-1 vector.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R. McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Sean R McGarry
Primary Examiner
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